SPECIAL SECTION: AGING AND INFECTIOUS DISEASES

Thomas T. Yoshikawa, Section Editor

Fever in the Elderly

Dean C. Norman

Department of Medicine, Division of Geriatrics, University of California of Los Angeles School of Medicine, and Veterans' Affairs–Greater Los Angeles Healthcare System

Infections in the elderly, similar to other acute illnesses in this age group, may present in atypical, nonclassical fashions. Fever, the cardinal sign of infection, may be absent or blunted 20%–30% of the time. An absent or blunted fever response may in turn contribute to diagnostic delays in this population, which is already at risk for increased morbidity and mortality due to infection. On the other hand, the presence of a fever in the geriatric patient is more likely to be associated with a serious viral or bacterial infection than is fever in a younger patient. Finally, a diagnosis can be made in the majority of cases of fever of unknown origin (FUO) in the elderly. FUO is often associated with treatable conditions in this age group.

Compared with the younger population, the elderly have increased susceptibility to infection and are at significantly increased risk for morbidity and mortality due to many common infections [1]. Possible explanations for the observed higher morbidity and mortality rates among older patients include low physiological reserves due to the biologic changes that accompany aging and the frequent presence of comorbid illnesses. Morbidity and mortality rates also are influenced by age and comorbidity-related decremental changes in host defenses. Older adults are at greater risk for hospitalization, which can in turn be complicated by nosocomial infection. The elderly are also at increased risk for adverse drug reactions; in clinical geriatrics, even with careful consideration, patients may be treated with multiple medications. In addition, there are biological changes that occur with age that alter the pharmacology of many classes of drugs, including antibiotics. Finally, delays in diagnosis and initiation of appropriate treatment due to atypical presentation may lead to increased morbidity and mortality.

Prevention, early recognition, and prompt initiation of empirical antimicrobial therapy are the cornerstones of the strategy to reduce the impact of infectious diseases on older adults. However, early recognition and avoidance of diagnostic delays may be problematic in this age group, since atypical presentations of acute diseases occur are common. Nonclassical presentation of infections is common in old age. Virtually any acute change in functional status may herald the onset of a serious infectious disease. For example, changes in cognitive function from baseline are commonly seen, even when the infection does not involve the CNS. Furthermore, pneumonia may present without cough or increased sputum production, and lower-tract urinary infection may occur without urgency, frequency, or dysuria [2, 3]. A common factor for all acute infections in the elderly is that up to one-third of patients may present without a robust febrile response [2, 3].

Normal and febrile body temperature for older adults. Even a young, healthy population shows wide variation in normal body temperature [4]. This is also true for the elderly, and only a few studies have established a normal body temperature for this age group [2, 3]. Coexisting chronic diseases, biological changes with normal aging, and the use of medications contribute to the broad physiological heterogeneity observed in the aged. Moreover, the measurement of body temperature is complicated by the effects of circadian rhythms and the site of measurement and method of thermometry.

Nevertheless, some generalizations can be made about normal body temperature in the elderly. A carefully controlled study of a small group of healthy older individuals (mean age, 59 years) and a much younger age group demonstrated that mean peak and nadir temperatures did not differ between the old and the young. However, the amplitude of circadian-rhythm temperature fluctuations was lower in the older group [5]. A consistent finding in more frail elderly patients is that baseline temperatures are lower than in healthy younger persons. Mean morning rectal temperature was 37.3°C, whereas mean morning oral temperature was 36.7°C in a study of 73 geriatric inpatients [6]. The standard deviation was 0.66°C for rectal temperatures and 0.8°C for oral temperatures.

Similarly, we found baseline body temperature to be reduced in frail nursing home residents [7]. Mean baseline morning rec-

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Reprints or correspondence: Dr. Dean C. Norman, Veterans' Affairs Medical Center West Los Angeles, 11301 Wilshire Blvd., Los Angeles, CA 90073 (Dean.Norman@Med.VA.Gov).

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tal temperature was 37°C in 22 patients whose oral temperatures could not be easily determined. The mean oral temperature of 85 other residents was 37.3°C. Diurnal variation was only 0.3°C for rectal temperatures and 0.2°C for oral temperatures. In another study [8], 74 afebrile hospitalized geriatric inpatients were similarly studied to determine the normal range of temperatures for the frail elderly. This study established the upward limits for normal temperatures: rectal, 37.5°C; oral, 37.3°C; axillary, 37°C; and proximal auditory canal, 37°C.

Although rectal temperature is touted as the "gold standard," rectal temperature measurement is often impractical in debilitated, noncooperative patients. Oral, sublingual temperature is the most common site of measurement, although recently the convenience of tympanic membrane (TM) temperature measurement has increased the popularity of this site. Oral temperature measurement may be affected by uncooperative and disturbed behaviors of patients with dementia or other neurobehavioral disorders, presence of tongue tremors, mouth-breathing, variations in the rate and depth of respiratory patterns, and ingestion of hot and cold fluids.

Further differences may occur in oral temperature measurement, depending on whether an electronic or a standard mercury-glass thermometer is used. In one study [9], 10% of fevers that were caught by electronic thermometers were missed by mercury-glass thermometers, and 95% of elderly patients with "definite" infection had fever that was defined as an oral temperature >37.2°C. The definition of "definite infection" was based on a scoring system, which appropriately did not have temperature as a criterion. The mean oral temperature of the febrile patients was 38°C by mercury-glass thermometer and 38.2°C by electronic thermometer. A further noteworthy finding was that the onset of pyrexia was delayed several hours in a significant number of patients and was delayed >12 h in 12% of patients. Thus, in some elderly patients who initially present with a blunted or absent febrile response, a febrile response may occur over time.

Downton et al. [6] compared the ability of oral, axillary, and rectal temperature measurements to detect fever in 73 geriatric patients admitted to a geriatric unit. Oral temperatures correlated more closely with variations in rectal temperatures than did axillary temperatures. Similar to findings in studies of younger populations, both oral and axillary temperatures tended to be lower (0.66°C and 0.88°C, respectively) than rectal temperatures. Further studies by Darowski et al. [10] demonstrated that in a "definitely infected" group of hospitalized elderly patients, rectal temperature measurement detected fever in 86% of patients (compared with 66% by sublingual and only 32% by axillary temperature measurement).

Many medical centers are switching to TM temperatures taken with infrared thermometers. Although there is a paucity of clinical data on the accuracy of TM thermometry in the elderly population, Castle et al. [11] demonstrated that TM temperatures were equivalent to or better than oral temperatures in correlating with rectal temperatures in a nursing home population. However, the study did not investigate the ability of TM thermometry to detect fever or measure temperatures outside the normal range of body temperatures for this age group. A more recent prospective study of 45 inpatients in an acute geriatric unit compared rectal and infrared ear temperatures. Although rectal temperature was higher than TM temperature (37.4°C vs. 36.9°C), there was a high positive correlation between rectal and TM temperatures. Moreover, TM temperature had acceptable sensitivity (86%) and specificity (89%) for detecting the presence of fever. Fever was defined by a rectal temperature of at least 37.6°C. A TM temperature of 37.2°C was used as the fever threshold [12].

On the basis of the above studies and additional studies described below, fever in the elderly can be defined as a persistent oral or TM temperature ⩾37.2°C or persistent rectal temperature ⩾37.5°C. Moreover, an increase over baseline temperature ⩾1.3°C, independent of site measured or device used, also indicates the presence of a fever. It should be remembered that any acute change in functional status, regardless of whether or not a fever is present, should lead to the consideration that an acute infection may be present.

Absent or blunted fever response in the elderly. There is ample evidence that a blunted fever response to a serious bacterial, viral, or fungal infection suggests a poorer prognosis than does a robust fever response [13]. In addition, there is a substantial body of data, mostly from animal models, that fever—through its effects on immune function—may be an important host defense mechanism [14]. Roughly 20%–30% of elderly persons with serious bacterial or viral infections will present with a blunted or entirely absent fever response [2, 3, 15]. In the old, bacteremia [16, 17], endocarditis [18, 19], pneumonia [20, 21], and meningitis [22] may present with lower fever than in the young. In a recent study of acute surgical abdomens in octogenarians, a substantial percentage of patients with acute cholecystitis, perforation, and appendicitis presented with temperatures <37.5°C [23]. Finally, a current study of the occurrence of nosocomial febrile illness in patients residing in an acute geriatric-medicine unit found that the mean "febrile" rectal temperature was only 38.1°C. The study's cutoff definition for a significant fever in this elderly population was a rectal temperature of 37.8°C. Only 8% of these febrile patients had rectal temperatures >38.5°C [24].

Pathogenesis of blunted fever response in the elderly. Difficulties in measuring temperature may result in spuriously low temperature readings in some cases in which fever is actually present. In addition, lower baseline temperatures observed in the elderly may lower the maximum temperature of a fever response to an infection. We examined 50 randomly selected nursing home residents and found that the mean oral baseline temperature was 36.3°C [25]. A retrospective review found 69 infections in 26 of these residents. The mean maximum temperature was 38.5°C, but in ~50% of these infected patients the

temperature did not reach 38.3°C. Many of these patients did have a "robust" change in temperature from baseline of at least 1.3°C.

A follow-up prospective study of 111 nursing home patients found that lowering the threshold for a clinically significant fever to an oral temperature of 37.8°C increased the sensitivity for detecting an infection to 70%. At 38.3°C the sensitivity was only 40% [7]. The sensitivity for detecting an infection increased to 83% when 37.2°C became the threshold, but the specificity dropped to 89%. The specificity was 99.7% when 38.5°C was the threshold and 98.3% when 37.8°C was used. Taken together, these findings indicate that elderly nursing home residents with a persistent oral temperature >37.2°C or an increase in body temperature of 1.3°C above baseline should be evaluated for the presence of infection. The likelihood of an infection is further increased if there are typical or classic signs and symptoms or if there is any change in functional status accompanying the temperature elevation.

The physiological mechanism(s) for the blunted temperature responses to infection observed in the elderly have not been clearly elucidated. However, the basic pathogenesis of fever is becoming more clear [26, 27] and suggests alterations that possibly accompany aging. Diminished thermoregulatory responses, such as sudomotor and vasomotor responses, as well as quantitative and qualitative abnormalities in both the production of and response to endogenous pyrogens, such as IL-1, IL-6, and TNF, may be possible explanations for the differences between elderly and young patients in fever response to infection.

Aging could also limit the ability of the hypothalamic circumventricular organs to allow endogenous pyrogens to cross from the blood stream to exert their effect on the CNS. Rodent models of aging have variably demonstrated diminished production of endogenous pyrogens [28, 29] but have more consistently demonstrated reduced fever response to iv injections of various endogenous mediators of fever, including IL-1, IL-6, and TNF [30–33]. Intracerebroventricular injection of IL-1 yielded similar immediate fever responses in young and in old rats, which suggests an inability of peripheral endogenous mediators to reach the CNS, rather than an unresponsiveness of the CNS [34]. Additional rodent experiments have suggested that changes in thermogenic brown fat that accompany aging may also play a role in blunted fever response [35]. In summary, animal data suggest that reduced production and response to endogenous pyrogens may play a role in the blunted febrile response to infection observed in the elderly.

Special significance of fever in the elderly. In older persons, a robust febrile response to infection has special significance. One large study of >1200 ambulatory patients demonstrated that an oral temperature of 38.3°C in elderly patients was usually due to a serious bacterial or viral infection [36]. Fever or at least an elevation of temperature over baseline will still occur in most cases of infection in the geriatric patient. However, unlike in the young, whose fevers are associated mostly with benign viral infections, in the elderly (especially those aged >80 years), oral temperatures reaching or exceeding 38.3°C will more likely be associated with serious bacterial or viral infections [36–38]. This can be expected to be particularly true for frail, debilitated patients. Therefore, as mentioned above, an infectious etiology should be sought in any such cases in which there is a change in functional status (e.g., worsening mental status) and in which the oral temperature is ⩾37.2°C or there has been a significant increase in temperature from baseline.

Table 1. Etiology of fever of unknown origin in a group of elderly and younger patients.

Etiology	Elderly (n = 204)	Young (n = 152)
Infection	72 (35)	33 (21)
Viral	1 (.05)	8 (5)
Tuberculosis	20 (10)	4 (3)
Abscess	25 (12)	6 (4)
Endocarditis	14 (7)	2 (1)
Other	12 (6)	13 (9)
Multisystem disease[a]	57 (28)	27 (17)
Tumor	38 (19)	8 (5)

NOTE. Data are no. (%) of patients. This table is adapted from the comparative study in [41].

[a] In descending order of frequency [41]: temporal arteritis, polymyalgia rheumatica, Wegener's granulomatosis, polyarteritis nodosa, rheumatoid arthritis, and sarcoidosis.

Fever of unknown origin. Past studies of fever of unknown origin (FUO) in the elderly have revealed that unlike for the young, a precise diagnosis can be made 87%–95% of the time [39–41]. In many cases, FUO is due to atypical presentations of common diseases [42]. Infection is the etiology in 25%–35% of cases, with tuberculosis occurring much more commonly in elderly than young patients with FUO. Connective-tissue diseases such as temporal arteritis, rheumatoid arthritis, and polymyalgia rheumatica cause 25%–31% of cases in elderly patients, and malignancy accounts for 12%–23% of cases [39, 41]. Table 1 summarizes this data. Since many of these diseases are treatable, it is well worth pursuing the etiology of FUO in the elderly.

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